

REMARKS

Applicants have entered into the present specification a substitute paper copy Sequence Listing section according to 37 C.F.R. §1.821(c) as new pages 1-10. The substitute Sequence Listing section contains clerical corrections in sections <110>, <130>, <140, 141>, and <150, 151> and in sections <223> of the sequences. Furthermore, attached hereto is a 3 1/2" disk containing the "Sequence Listing" in computer readable form in accordance with 37 C.F.R. §1.821(e).

Applicants have amended the specification to insert SEQ ID Nos, as supported in the present specification.

The following statement is provided to meet the requirements of 37 C.F.R. §1.825(a) and 1.825(b).

I hereby state, in accordance with 37 C.F.R. §1.825(a), that the amendments included in the substitute sheets of the sequence listing are believed to be supported in the application as filed and that the substitute sheets of the sequence listing are not believed to include new matter.

I hereby further state, in accordance with 37 C.F.R. §1.825(b), that the attached copy of the computer readable form is the same as the attached substitute paper copy of the sequence listing.

Under U.S. rules, each sequence must be classified in <213> as an "Artificial Sequence", a sequence of "Unknown" origin, or a sequence originating in a particular organism, identified by its scientific name.

Neither the rules nor the MPEP clarify the nature of the relationship which must exist between a listed sequence and an organism for that organism to be identified as the origin of the sequence under <213>.

Hence, counsel may choose to identify a listed sequence as associated with a particular organism even though that sequence does not occur in nature by itself in that organism (it may be, e.g., an epitopic fragment of a naturally occurring protein, or a cDNA of a naturally occurring mRNA, or even a substitution mutant of a naturally occurring sequence). Hence, the identification of an organism in <213> should not be construed as an admission that the sequence *per se* occurs in nature in said organism.

Similarly, designation of a sequence as "artificial" should not be construed as a representation that the sequence has no association with any organism. For example, a primer or probe may be designated as "artificial" even though it is necessarily complementary to some target sequence, which may occur in nature. Or an "artificial" sequence may be a substitution mutant of a natural sequence, or a chimera of two or more natural sequences, or a cDNA (i.e., intron-free sequence) corresponding to an intron-containing gene, or otherwise a fragment of a natural sequence.

The Examiner should be able to judge the relationship of the enumerated sequences to natural sequences by giving full consideration to the specification, the art cited therein, any further art cited in an IDS, and the

results of his or her sequence search against a database containing known natural sequences.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made".

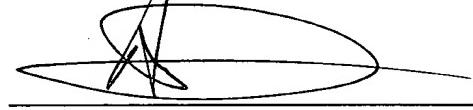
Applicants submit that the present application contains patentable subject matter and therefore urge the examiner to pass the case to issuance.

If the examiner has any questions or comments concerning the above described application, the examiner is urged to contact the undersigned at the phone number below.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification:

A substitute specification has been submitted.

In the claims:

Claims 4 and 6-10 have been amended as follows:

4 (Amended). A synthetic peptide according to any one of claim 1, selected from:

(i) peptides **pep1**, **pep2**, and **pep3** of the sequences:

(**pep1**) Ile-Val-Leu

(**pep2**) Glu-Phe-Leu-Asn-Arg-Trp-Ile-Thr (SEQ ID NO:1)

NO:1)

(**pep3**) Arg-Met-Leu-Thr (SEQ ID NO:2)

(ii) peptides obtained from **pep2** by deletion of one or more amino acid residues;

(iii) peptides obtained by addition to peptides (i) or (ii) of one or more natural or non-natural amino acid residues;

(iv) peptides obtained by replacement of one or more amino acid residues of peptides (i) to (iii) by the corresponding D-stereomer, by another natural amino acid residue or by a non-natural amino acid residue;

(v) chemical derivatives of the peptides (i) to (iv);

(vi) cyclic derivatives of peptides (i) to (v);

(vii) dual peptides consisting of two of the same or different peptides (i) to (vi), wherein the peptides are covalently linked to one another directly or through a spacer; and

(viii) multimers comprising a number of the same or different peptides (i) to (vi).

6 (Amended). A synthetic peptide according to claim 5, selected from:

- (pep1) Ile-Val-Leu
- (pep4) Asn-Ile-Asn-Val-Ile-Val-Leu (SEQ ID NO:3),
- (pep5) Ile-Val-Leu-Glu-Leu-Lys-Gly (SEQ ID NO:4),
- (pep6) Asn-Val-Ile-Val-Leu (SEQ ID NO:5)
- (pep7) Ala-Val-Leu
- (pep8) Ile-Ala-Leu
- (pep9) Ile-Val-Ala
- (pep10) Glu-Val-Leu
- (pep11, linear) and (pep12, cyclic) Cys-Ile-Val-Leu-Ala-Cys (SEQ ID NO:6) and,
- (pep13, linear) and (pep14, cyclic) Cys-Ile-Val-Leu-Ala-Ala-Cys (SEQ ID NO:7).

7 (Amended). The synthetic peptide Glu-Phe-Leu-Asn-Arg-Trp-Ile-Thr (SEQ ID NO:1) (pep2), and derivatives thereof according to claim 4, obtained by:

- (a) elongation by up to 4 further amino acid residues at the C and/or N terminal ends, preferably according to the natural sequence of IL-2;
- (b) substitution of the Glu residue by a natural or non-natural charged or polar charged amino acid residue, preferably selected from Lys, Arg, Asp, Gln, Asn;
- (c) substitution of the Phe residue by a natural or non-natural hydrophobic aliphatic or aromatic amino acid

residue, preferably selected from Ala, Val, Ile, Leu, Tyr, Trp, Phe, Met, Nle;

(d) substitution of the Leu residue by a natural or non-natural hydrophobic aliphatic or aromatic amino acid residue, preferably selected from Ala, Val, Ile, Leu, Tyr, Trp, Phe, Met, Nle;

(e) substitution of the important Asn residue by a hydrophilic, non-charged, aliphatic natural or non-natural amino acid residue such as Gln;

(f) substitution of the Arg residue by a positively charged, natural or non-natural amino acid residue, preferably selected from Lys, Orn, homoArg;

(g) substitution of the Trp residue by a natural or non-natural hydrophobic, aliphatic or aromatic, amino acid residue, preferably selected from Tyr, Ile, Leu, Nle, Tic, Phe, 4-phenyl-Phe, 4-methyl-Phe;

(h) substitution of the Ile residue by a natural or non-natural hydrophobic, aliphatic or aromatic, amino acid residue, preferably selected from Tyr, Phe, Leu, Nle, Tic;

(i) substitution of the Thr residue by an aliphatic hydrophobic amino acid residue such as Ala, Ile, Leu, or a hydroxy- or thio-containing amino acid residue preferably selected from Cys, Ser;

(j) truncation by up to 4 amino acid residues from either the C or N terminal;

(k) amidation of the C-terminal Thr;

(l) cyclization of pep2 or of any peptide of (a) to (k); and

(m) any combination of (a) to (l).

8 (Amended). A peptide according to claim 7,
selected from:

(pep2) Glu-Phe-Leu-Asn-Arg-Trp-Ile-Thr (SEQ ID NO:1)

(pep15) Ile-Val-Glu-Phe-Leu-Asn-Arg-Trp-Ile-Thr
(SEQ ID NO:8)

(pep16) Glu-Phe-Leu-Asn-Arg-Trp-Ile-Thr-Phe-Cys
(SEQ ID NO:9)

(pep17) Ala-Thr-Ile-Val-Glu-Phe-Leu-Asn-Arg-Trp-
Ile-Thr (SEQ ID NO:10)

(pep18) Glu-Phe-Leu-Asn-Arg-Trp-Ile-Thr-Phe-Cys-
Gln-Ser (SEQ ID NO:11)

(pep19) Leu-Asn-Arg-Trp-Ile-Thr (SEQ ID NO:12)

(pep20) Arg-Trp-Ile-Thr (SEQ ID NO:13)

(pep21) Glu-Phe-Leu-Asn (SEQ ID NO:14)

(pep22) Ala-Phe-Leu-Asn-Arg-Trp-Ile-Thr (SEQ ID NO:15)

(pep23) Lys-Phe-Leu-Asn-Arg-Trp-Ile-Thr (SEQ ID NO:16)

(pep24) Glu-Ala-Leu-Asn-Arg-Trp-Ile-Thr (SEQ ID NO:17)

(pep25) Glu-Val-Leu-Asn-Arg-Trp-Ile-Thr (SEQ ID NO:18)

(pep26) Glu-Phe-Ala-Asn-Arg-Trp-Ile-Thr (SEQ ID NO:19)

(pep27) Glu-Phe-Leu-Ala-Arg-Trp-Ile-Thr (SEQ ID

NO:20)

(pep28) Glu-Phe-Leu-Asn-Ala-Trp-Ile-Thr (SEQ ID

NO:21)

(pep29) Glu-Phe-Leu-Asn-Glu-Trp-Ile-Thr (SEQ ID

NO:22)

(pep30) Glu-Phe-Leu-Asn-Arg-Ala-Ile-Thr (SEQ ID

NO:23)

(pep31) Glu-Phe-Leu-Asn-Arg-Trp-Ala-Thr (SEQ ID

NO:24)

(pep32) Glu-Phe-Leu-Asn-Arg-Trp-Ile-Ala (SEQ ID

NO:25)

(pep33) Glu-Phe-Leu-Asn-Arg-Trp-Ile-Thr-NH₂ (SEQ ID

NO:26) and,

(pep34, linear) and (pep35, cyclic) Cys-Glu-Phe-Leu-Asn-Arg-Trp-Ile-Thr-Ala-Cys (SEQ ID NO:27).

9 (Amended). The synthetic peptide Arg-Met-Leu-Thr (SEQ ID NO:2) (pep3), and derivatives thereof according to claim 4, obtained by:

(a) elongation by up to 4 further amino acid residues at the C and/or N terminal end, preferably according to the natural sequence of IL-2;

(b) substitution of the Arg residue by a natural or non-natural positively charged amino acid residue, preferably selected from Lys, Orn, homoArg, diaminobutyric acid;

(c) substitution of the Met residue by a natural or non-natural hydrophobic, aliphatic or aromatic, amino acid

residue, preferably selected from Phe, Tyr, Ile, Leu, Nle, Tic;

(d) substitution of the Leu residue by a natural or non-natural hydrophobic, aliphatic or aromatic, amino acid residue, preferably selected from Phe, Tyr, Nle, Tic;

(e) substitution of the Thr residue by an aliphatic hydrophobic amino acid residue such as Ala, Ile, Leu, or a hydroxy- or thio-containing amino acid residue such as Ser, Cys;

(f) amidation of the C-terminal Thr residue;

(g) cyclization of **pep3** or of any peptide of (a) to (f); and

(h) any combination of (a) to (g).

10. (Amended). A peptide according to claim 9, selected from:

(**pep3**) Arg-Met-Leu-Thr (SEQ ID NO:2)

(**pep36**) Ala-Met-Leu-Thr (SEQ ID NO:28)

(**pep37**) Arg-Ala-Leu-Thr (SEQ ID NO:29)

(**pep38**) Arg-Met-Ala-Thr (SEQ ID NO:30)

(**pep39**) Arg-Met-Leu-Ala (SEQ ID NO:31)

(**pep40**) Lys-Met-Leu-Thr (SEQ ID NO:32)

(**pep41**) Arg-Val-Leu-Thr (SEQ ID NO:33)

(**pep42**) Arg-Met-Leu-Thr-NH₂ (SEQ ID NO:34)

(**pep43**) Pro-Lys-Leu-Thr-Arg-Met-Leu-Thr (SEQ ID NO:35)

(**pep44**) Arg-Met-Leu-Thr-Phe-Lys-Phe-Tyr (SEQ ID NO:36) and,

(pep45, linear) and (pep46, cyclic) Cys-Arg-Met-
Leu-Thr-Ala-Cys (SEQ ID NO: 37).